

Amendments to the Claims

This listing of claims replaces all prior versions and listings of claims in the application.

Listing of Claims:

1. (Currently amended) A composition comprising a ~~polypeptide in~~ crystalline form ~~of, wherein the polypeptide is~~ a TNF- α -converting enzyme (TACE) polypeptide, ~~and wherein~~ the crystalline form of the TACE polypeptide crystal is of monoclinic space group P2₁ and has unit cell dimensions a=61.38 Å, b=126.27 Å, c=81.27 Å, and β =107.41°.

2. (Previously presented) A composition according to claim 1, wherein the TACE polypeptide comprises a TACE catalytic domain (TCD).

3. (Original) A composition according to claim 1, wherein the TACE polypeptide is the expression product of a polynucleotide encoding a pro domain and a catalytic domain of TACE.

4. (Original) A composition according to claim 1, wherein the TACE polypeptide is the expression product of a polynucleotide encoding amino acid residues 1-477 of TACE as set forth in SEQ ID NO:8.

5. (Currently amended) A composition according to claim 4, wherein the expression product of the polynucleotide is further substituted such that amino acid residue Ser266 as set forth in SEQ ID NO:8 is changed to Ala and amino acid residue ~~Asn542~~ Asn452 as set forth in SEQ ID NO:8 is changed to Gln, and wherein ~~a second polynucleotide encoding sequence the sequence~~ Gly-Ser-(His)₆ (SEQ ID NO:2) is fused to the C-terminus of the expression product.

6. (Cancelled)

7. (Currently amended) A composition according to claim ~~[[6]]~~ 1, ~~wherein the binding partner is~~ further comprising a hydroxamate-based binding partner.

8. (Currently amended) A composition according to claim ~~[[6]]~~ 7, wherein the hydroxamate-based binding partner is N-{D,L-2-(hydroxyaminocarbonyl)methyl-4-methylpentanoyl}-L-3-amino-2-dimethylbutanoyl-L-alanine,2-(amino)ethyl amide.

9. (Currently amended) A composition according to claim 1, wherein the crystal diffracts x-rays to 2.0 Å.

10. (Canceled)

11. (Currently amended) A composition according to claim ~~2~~ 4, wherein the unit cell of the crystal comprises four crystallographically independent TACE catalytic domains ~~domain~~ (TCD) ~~molecules of the TACE polypeptide.~~

12. (Currently amended) A composition according to claim 11, wherein the TACE catalytic domains of the TACE polypeptide ~~TCD molecules~~ are in an asymmetric unit.

13. (Cancelled)

14. (Currently amended) A composition according to claim 1, wherein the ~~the~~ crystalline form of the TACE polypeptide ~~crystal~~ has the structure coordinates according to Table 1.

15. (Currently amended) A method for crystallizing a TACE polypeptide, comprising:

(A) mixing a solution comprising:

(i) a TACE polypeptide, wherein the TACE polypeptide is the expression product of a polynucleotide encoding amino acid residues 1-477 of TACE as set forth in SEQ ID NO:8; and

(ii) a hydroxamate-based binding partner,

with a crystallization buffer, wherein the crystallization buffer comprises sodium citrate; and

(B) crystallizing the mixture of step (A) by drop vapor diffusion to form a crystalline precipitate.

16. (Original) The method according to claim 15, further comprising:
(C) transferring seeds from the crystalline precipitate formed by the drop vapor diffusion, along with a crystallization promoter, into a mixture of a concentrated solution comprising a TACE polypeptide and binding partner substrate, and a crystallization buffer; and
(D) crystallizing the mixture of step (C) by drop vapor diffusion to form a crystal.
17. (Currently amended) The method of claim 15, wherein said crystallization buffer is selected from the group consisting of 0.1M Na Citrate pH 5.4, 20% w/v PEG 4000, and 20% v/v isopropanol; 0.1 M Na Citrate pH 5.0 and 40% v/v ethanol; and 0.1M Na Citrate pH 8.7, 20% w/v PEG 4000, and 20% v/v isopropanol.
18. (Currently amended) The method of claim 15, wherein the hydroxamate-based binding partner is N-{D,L-2-(hydroxyaminocarbonyl)methyl-4-methylpentanoyl}-L-3-amino-2-dimethylbutanoyl-L-alanine, 2-(amino)ethyl amide N-{D,L-2-(hydroxyaminocarbonyl)methyl-4-methylpentanoyl}-L-3-amino-2-dimethylbutanoyl-L-alanine, 2-(amino)ethyl amide.
19. (Original) The method of claim 15, wherein crystallization is at a temperature ranging from 4 to 20 degrees Celsius.
20. (Original) The method of claim 15, wherein the solution comprising the TACE polypeptide and the binding partner is at a concentration of about 5 mg/mL to about 12 mg/mL in a buffer.
21. (Original) The method of claim 20, wherein the solution is mixed with the crystallization buffer in a 1:1 ratio.
22. (Previously presented) A TACE crystal made by co-crystallizing a TACE polypeptide with a ~~co-crystallization substrate~~ hydroxamate-based binding partner, wherein the TACE crystal is of monoclinic space group P2₁ and has the unit cell dimensions a=61.38 Å, b=126.27 Å, c=81.27 Å, and β=107.41°.
- 23-28. (Canceled)

29. (Original) The TACE crystal of claim 22, wherein the TACE polypeptide is the expression product of a polynucleotide encoding comprises amino acid residues 1-477 of TACE as set forth in SEQ ID NO:8.

30. (Currently amended) The TACE crystal of claim 22, wherein the crystal of the TACE polypeptide has the structure coordinates according to Table 1.

31. (Currently amended) The TACE crystal of claim 22, wherein the hydroxamate-based binding partner-substrate is N-{D,L-2-(hydroxyaminocarbonyl)methyl-4-methylpentanoyl}-L-3-amino-2-dimethylbutanoyl-L-alanine, 2-(amino)ethyl amide N-{D,L-2-(hydroxyaminocarbonyl)methyl-4-methylpentanoyl}-L-3-amino-2-dimethylbutanoyl-L-alanine, 2-(amino)ethyl amide.

32. (New) A composition comprising a crystalline form of a TNF- α -converting enzyme (TACE) polypeptide and a hydroxamate-based binding partner, wherein:

- (i) the crystalline form is of monoclinic space group P2₁; and
- (ii) the TACE polypeptide is the expression product of a polynucleotide encoding amino acid residues 1-477 of TACE as set forth in SEQ ID NO:8.

33. (New) The composition of claim 32, wherein the crystalline form of the TACE polypeptide and hydroxamate-based binding partner diffracts x-rays to 2 Å, and has a unit cell comprising four crystallographically independent TACE catalytic domains (TCDs) in an asymmetric unit.

34. (New) The composition of claim 33, wherein the crystalline form of the TACE polypeptide and hydroxamate-based binding partner has the structure coordinates according to Table 1.

35. (New) The composition of claim 34, wherein the hydroxamate-based binding partner is N-{D,L-2-(hydroxyaminocarbonyl)methyl-4-methylpentanoyl}-L-3-amino-2-

dimethylbutanoyl-L-alanine, 2-(amino)ethyl amide.

36. (New) The composition of claim 35, wherein the crystalline form the crystalline form of the TACE polypeptide and hydroxamate-based binding partner has unit cell dimensions $a=61.38 \text{ \AA}$, $b=126.27 \text{ \AA}$, $c=81.27 \text{ \AA}$, and $\beta=107.41^\circ$.